CRITERIA

Diagnosis of arrhythmogenic right ventricular dysplasia/cardiomyopathy

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Accepted for publication 1 December 1993

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Right ventricular dysplasia or cardiomyopathy is a heart muscle disorder of unknown cause that is characterised pathologically by fibrofatty replacement of the right ventricular myocardium.[1–5] Segmental right ventricular disease is usual, but evolution to more diffuse right ventricular involvement and left ventricular abnormalities with heart failure have been described.[6–10] The incidence is unknown. Clinical manifestations of the disease include structural and functional abnormalities of the right ventricle, electrocardiographic depolarisation/repolarisation changes, and presentation with sudden death or arrhythmias of right ventricular origin. The disease is often familial (about 30%) with an autosomal dominant inheritance.[11 12] It remains unclear whether this genetic background predisposes to a degenerative disease with atrophy and fibrofatty replacement of the right ventricular myocardium, or whether the inflammatory cells seen in approximately 25% of cases indicate an infectious or possibly genetically determined immune pathogenesis.[13]

Uncertainty concerning the pathogenesis of right ventricular dysplasia leads to the as yet unresolved question of whether it is a single entity or the common end point of several disease processes. The familial nature of many cases has led to recognition that in any particular family the phenotypic expression of the disease can be very variable. In turn this leads to the need for criteria to delineate the spectrum of disease that justifiably can be called right ventricular dysplasia in clinical practice.

A definitive (gold standard) diagnosis of right ventricular dysplasia is based on histological demonstration of transmural fibrofatty replacement of right ventricular myocardium at either necropsy (figs 1 and 2) or surgery.[14 15] In most patients, however, assessment of transmural myocardium is not possible.

Diagnosis based on right ventricular endomyocardial biopsy specimens is inherently difficult because the segmental nature of the disease causes false negatives and because the interventricular septum is rarely involved. Biopsy specimens cannot reflect transmural changes and not infrequently in normal subjects there are islands of adipose tissue between myocytes in the right ventricle. Nevertheless the positive finding of fibrofatty

Criteria for diagnosis of right ventricular dysplasia

I Global and/or regional dysfunction and structural alterations[17–23]*

MAJOR
Severe dilatation and reduction of right ventricular ejection fraction with no (or only mild) LV impairment
Localised right ventricular aneurysms (akinetic or dyskinetic areas with diastolic bulging)
Severe segmental dilatation of the right ventricle

MINOR
Mild global right ventricular dilatation and/or ejection fraction reduction with normal left ventricle
Mild segmental dilatation of the right ventricle
Regional right ventricular hypokinesia

II Tissue characterisation of walls

MAJOR
Fibrofatty replacement of myocardium on endomyocardial biopsy

III Repolarisation abnormalities

MINOR
Inverted T waves in right precordial leads (V2 and V3) (people aged more than 12 yr; in absence of right bundle branch block)

IV Depolarisation/conduction abnormalities

MAJOR
Epsilon waves or localised prolongation (>110 ms) of the QRS complex in right precordial leads (V1–V3)

MINOR
Late potentials (signal averaged ECG)

V Arrhythmias

MINOR
Left bundle branch block type ventricular tachycardia (sustained and non-sustained) (ECG, Holter, exercise testing).
Frequent ventricular extrasystoles (more than 1000/24 h) (Holter)

VI Family history

MAJOR
Familial disease confirmed at necropsy or surgery

MINOR
Familial history of premature sudden death (<35 yr) due to suspected right ventricular dysplasia.
Familial history (clinical diagnosis based on present criteria)

*Detected by echocardiography, angiography, magnetic resonance imaging, or radionuclide scintigraphy. ECG, electrocardiogram; LV, left ventricle.

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replacement of myocytes on biopsy can be a valuable diagnostic pointer. Diagnosis, however, relies heavily on the clinical demonstration of structural, functional, and electrophysiological abnormalities that are caused by or reflect the underlying histological changes.

Problems in the assessment of right ventricular structure and function, the multiple potential aetiologies of arrhythmias of right ventricular origin, and difficulties in the interpretation of the right ventricular endomyocardial biopsy have all made the establishment of definitive diagnostic criteria necessary.[16] The importance of a common approach to diagnosis led to the development of the task force and the following proposals for the establishment of diagnostic criteria. These are based on the identification of structural abnormalities, fatty or fibrofatty replacement of the right ventricular myocardium, electrocardiographic changes, arrhythmias of right ventricular origin, and familial disease.

It is proposed that the diagnosis of right ventricular dysplasia would be fulfilled by the presence from different groups (table) of:

Two major criteria
or
One major plus two minor criteria
or
Four minor criteria

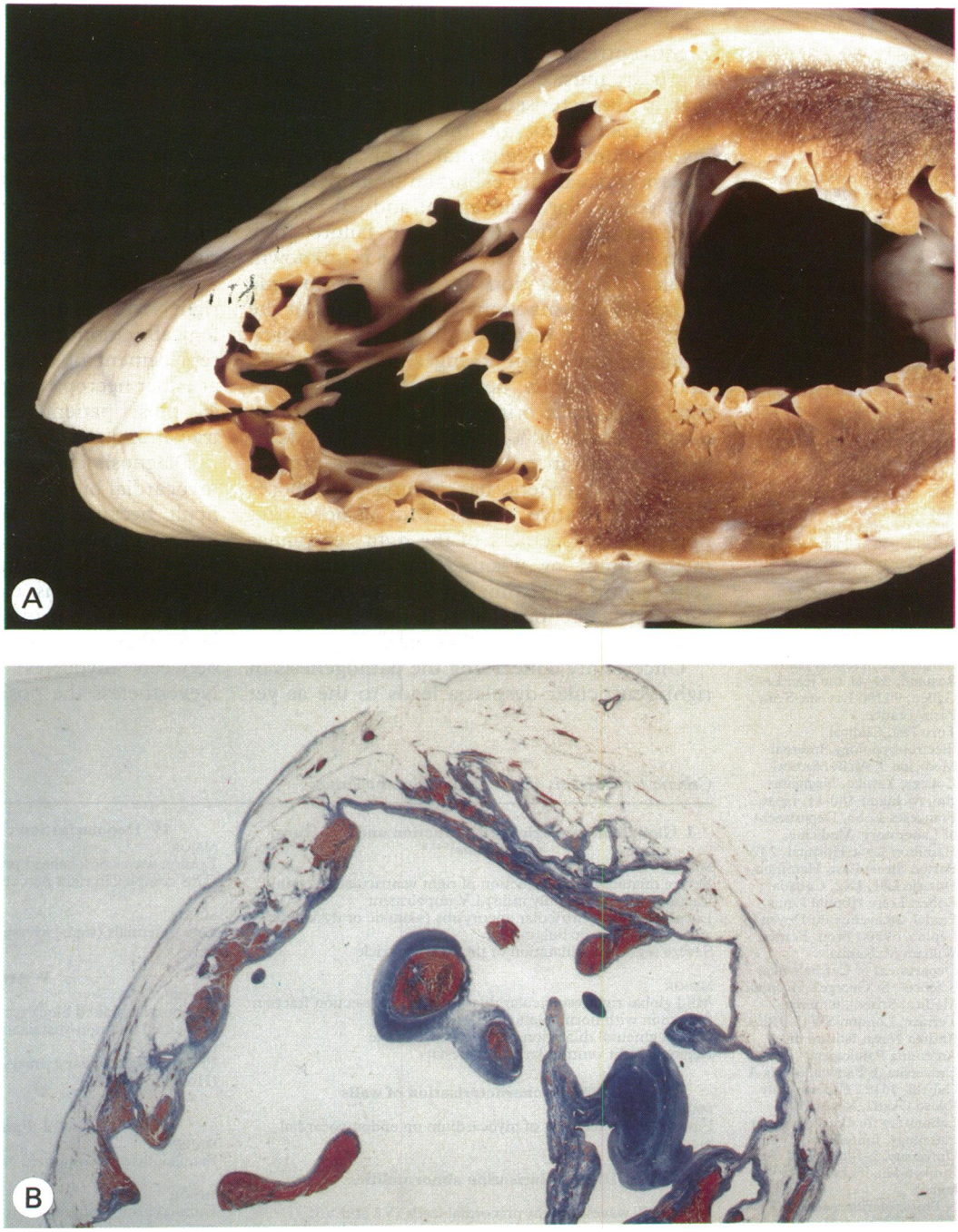

Figure 1 Necropsy findings in a 39 year old man with a family history of sudden death (two brothers) who had complex arrhythmia and died suddenly. (A) Cross section of the heart showing pronounced adipose infiltration of the right ventricular free wall and nearly normal left ventricle and ventricular septum. (B) Histological view of the right ventricular free wall showing myocardial atrophy and massive fibrofatty replacement. (Azan; original magnification, × 1.)

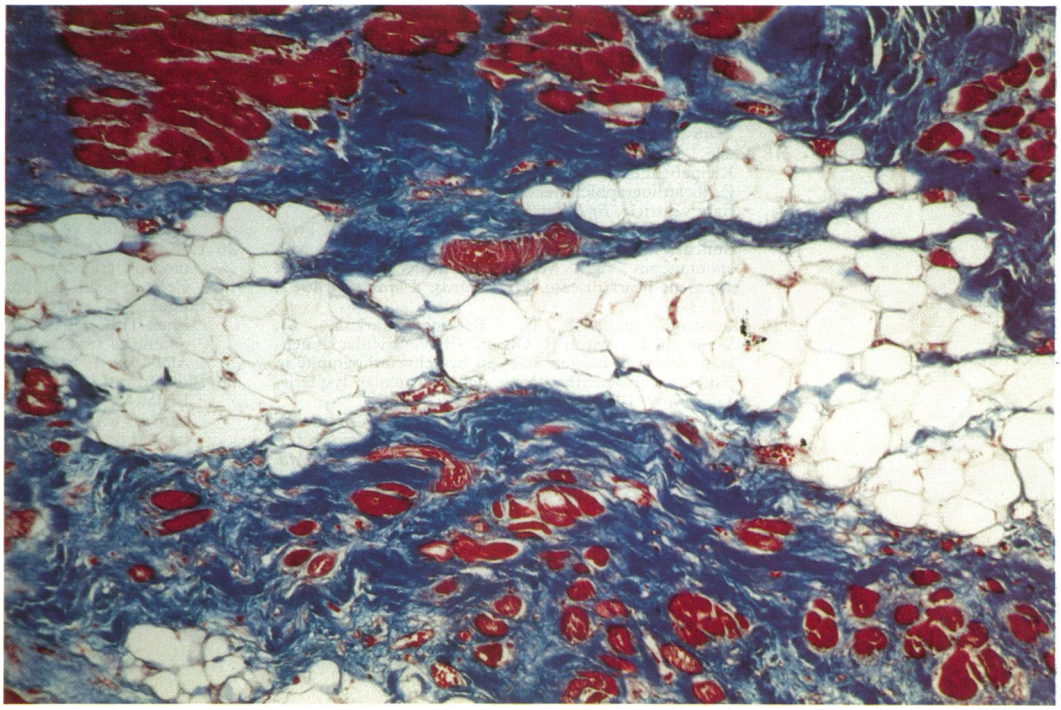

Figure 2 Histological view of the right ventricular free wall at high magnification, showing fibrofatty replacement. (Azan; original magnification, × 25.)

Dilatation of the right ventricle or segments of the right ventricle is defined by echocardiographic or angiographic dimensions that are two to three (mild) or ⩾three standard deviations from normal.[17–23] Problematic areas of interpretation are those where a subjective assessment is required, such as regional right ventricular dysfunction and structural alterations. Right ventricular endomyocardial biopsy on its own must be regarded as non-diagnostic, although when fibrofatty replacement is shown[24] biopsy may help with in vivo histological validation of the clinical diagnosis. Experience with magnetic resonance imaging and ultra-fast computed tomography in the diagnosis of right ventricular dysplasia is limited and requires further evaluation.[25,26]; preliminary studies suggest that it may be possible to distinguish between fat and myocardium. Conventional definitions are used for epsilon waves, an abnormal signal averaged electrocardiogram based on time analysis, and ventricular arrhythmias.[27–29]

The diagnosis of arrhythmogenic right ventricular dysplasia based on the presence of major and minor criteria encompassing structural, histological, electrocardiographic, arrhythmic, and genetic factors is presented as a working framework to improve understanding of this condition. We expect that with increased pedigree ascertainment the potential identification of the gene(s) responsible, and a more detailed understanding of the natural history our concepts will evolve to either a more succinct clinico-pathological diagnosis or ideally a diagnosis based on a specific gene abnormality. At present, however, a common approach to diagnostic criteria for a phenotypic expression of right ventricular dysplasia will be essential, both to clinical management and to scientific progress.

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